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EXAMINER
WALLENHORST, MAUREEN

ART UNIT	PAPER NUMBER
1797	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/563,817	REBOUD ET AL.	
	Examiner	Art Unit	
	Maureen M. Wallenhorst	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/6/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

2. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

3. The abstract of the disclosure is objected to because of the inclusion of legal phraseology such as "comprising". Correction is required. See MPEP § 608.01(b).

4. The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
    (1) Field of the Invention.
    (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).

(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

5. The disclosure is objected to because of the following informalities: There is no brief description of the drawings in the specification. In addition, there are no headings for the "Background of the Invention", the "Brief Summary of the Invention", the "Brief Description of the Drawings" and the "Detailed Description of the Invention".

Appropriate correction is required.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 35-69 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method and device for analyzing a reaction medium containing live cells that comprises a cell or cells in a solution of culture medium that has been deposited onto a planar support, and wherein the planar support is covered with a separating film that allows gases to pass through but prevents evaporation of the culture medium deposited on the support and the support is contained within a controlled-atmosphere chamber so as to allow the survival of the cells, does not reasonably provide enablement for the same method and device wherein the cells are not recited as being located within an aqueous solution of a culture medium and the support is not recited as being located within a controlled-atmosphere chamber so as to allow the survival of the cells. The specification does not enable any person skilled in the art to which it pertains,

or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The specification of the instant application describes the invention as a method and device for analyzing live cells that are deposited in a drop of culture medium onto a planar support. In order for the cells to remain alive and viable during the testing, the cells must be located within some type of culture medium that provides the nutrients and other reagents needed to maintain the proliferation and growth of the cells. See page 20 of the instant specification. In addition, the planar support on which the live cells are deposited for testing in a mass spectrometer must be located within a controlled-atmosphere chamber that allows the survival of the cells by providing the correct temperature, hygrometry and carbon dioxide content for the cells. Without the presence of a culture medium containing the proper nutrients for the cells to survive and without the presence of a controlled atmosphere chamber for holding the planar support to provide the proper temperature and gaseous conditions for the cells to survive, the cells tested in the method and device of the instant invention would not remain viable. Therefore, in order for the claims to be fully enabled under 35 USC 112, first paragraph, the cells must be recited as being suspended in a culture medium, and the support on which the cells are deposited must be recited as being located within a controlled atmosphere chamber. It is noted that while instant claims 52-54 recite a controlled atmosphere chamber and claim 61 recites the cells in a culture medium, it is the combination of both of these limitations that must be present in each of the claims in order for the claims to be enabled under 35 USC 112, first paragraph.

8. Claims 35-69 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 35 is indefinite since there is no step (iii) in the method following step (ii) and before step (iv). In step (iv) of claim 35, the recited "reaction medium" is indefinite since it is not clear whether the reaction medium comprises the combination of the cell C in the aqueous drop on the support S, or whether it refers to only the cell C since the preamble of claim 35 recites the reaction medium as comprising at least one cell C. See this same problem in steps (v) and (vi) of claim 35, and in claims 43, 45, 46, 48 and 49. In step (iv) of claim 35, the phrase "the mass spectrometer" lacks antecedent basis. Steps (v) and (vi) of claim 35 are indefinite since it is not clear whether these steps take place in the mass spectrometer.

It is suggested to positively recite the steps in independent claim 35 as steps (i)-(v), and for the limitation of claim 36, to recite that before the step (iii) of preparing and introducing the reaction medium into a mass spectrometer, the cell C is subjected to a stimulation.

Claim 39 is indefinite since it depends from claim 35, and claim 35 does not recite the depositing of any reagent onto the support S. See this same problem in claim 40.

On line 2 of claim 50, the phrase "the data" lacks antecedent basis.

On line 5 of claim 51, the phrase "the aqueous drops" lacks antecedent basis and is indefinite since it is not clear whether the aqueous drops contain cells therein. On line 8 of claim 51, the recited "reaction medium" is indefinite since it is not clear whether the reaction medium comprises the combination of the cell C in the aqueous drop on the support S, or whether it refers

to only the cell C since the preamble of claim 51 recites the reaction medium as comprising at least one cell C.

On line 6 of claim 55, the phrase "the cavities" lacks antecedent basis.

Claim 62 is indefinite since it is not clear whether the recited "means" are the "means for depositing" or the "means for desorbing and ionizing" as recited in claim 51, or both.

In claim 67, the phrase "the means of measuring the mass" lacks antecedent basis since independent claim 51 recites a mass spectrometer.

9. Claims 68-69 are indefinite since these are method claims that have no steps other than to use the device as recited in claim 51. Claims 68-69 provide for the use of the device of claim 51 to identify modifications in cells and to study changes in cells over time, but, since the claims do not set forth any steps involved in the method/process other than using the device of claim 51, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 68-69 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. Claims 35-39 and 41-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al (EP 1,284,496, submitted in the IDS filed on January 6, 2006) in view of Schaack et al. (WO 2004/011938).

Brown et al teach of a method and device for analyzing a sample using matrix-assisted laser desorption ionization-time-of-flight (MALDI-TOF) mass spectrometry. The sample to be analyzed can comprise cells. The device comprises a support 1 having a planar surface (claims 35, 51, 68-69). The support 1 is comprised of a flat conductive metal plate or glass plate 2 having a hydrophobic material coated thereon (claims 56-57). Laser etched portions 3 are

arranged on the plate 2 in an array formation for receiving a sample of cells in each of the portions using surface tension forces (claims 38, 58-59, 63). The sample plate can be washed once the samples are deposited onto the plate and prior to mass analysis (claims 43-44). A matrix solution containing an acid such as alpha-cyano-4-hydroxcinnamic acid (CHCA) is added to the samples on the plate after washing, and the combination of matrix material and samples are subsequently dried (claims 45-48). During the drying, crystal growth of the matrix is induced and analyte molecules become co-crystallized with the matrix. The MALDI sample plate is then inserted into a mass spectrometer tube that conventionally applies a vacuum and an electric field to the plate, and where a laser beam causes photon bombardment of the matrix material to desorb and ionize the analyte molecules. The desorbed ions are then mass analyzed in the mass spectrometer (claims 49, 64-67). The measured mass spectra data is compared to reference spectra for identifying the cells, biomolecules, etc. in the samples (claim 50). Brown et al also teach that another embodiment of a known MALDI plate comprises a stainless steel plate coated with a hydrophobic Teflon material that has a plurality of hydrophilic gold spots thereon for receiving samples to be analyzed (claim 59). See Figures 1a, 1b and 2, and paragraphs 0001-0004, 0007, 0017, 0057-0063, 0067-0070, and the claims of Brown et al. Brown et al fail to teach that the planar surface of the support 1 is covered with a film after a sample containing cells is applied thereto for allowing gases to pass through while preventing evaporation of the aqueous solution in which the cells are located.

Schaack et al teach of a method and device for screening molecules in cells. The method comprises setting a cell C onto the planar surface of a support S using a capillary-type device in the form of an aqueous drop. The planar surface of the support S where the aqueous drop of the

cell is set is then covered with a separation film F that allows gases to flow there through but prevents the aqueous drops on the support from evaporating. A reagent R is then dispensed into the aqueous drop of the cell for reaction with the cell by a capillary tube. See the English language abstract and the Figures in Schaack et al. Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15. The reference to Schaack et al qualifies as prior art under 35 USC 102(a) since it was published before the effective filing date of the instant application (i.e. before July 9, 2004), and a translation of Applicants' foreign priority document has not been received.

Based upon the combination of Brown et al and Schaack et al, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to provide the planar surface of the support in the device taught by Brown et al with a film after a sample containing cells is applied thereto for allowing gases to pass through while preventing evaporation of the aqueous solution in which the cells are located since Schaack et al teach that such a film on a planar support serves to keep live cells on the support viable by allowing gases needed for cell growth to pass into and out of the aqueous solution containing the cells while preventing the aqueous solution from evaporating, and Brown et al teach that the MALDI sample plate can be used to analyze live cells. With regards to claims 36-37 and 41-42, it would have been obvious to one of ordinary skill in the art to subject the cells taught by Brown et al on the MALDI sample plate to a stimulus such as a reagent molecule since Schaack et al teach that the interaction of cells with different molecules can be advantageously screened using a planar support-type of device, similar to the MALDI plate taught by Brown et al. With regards to claims 52-54, it

would have been obvious to one of ordinary skill in the art to place the MALDI sample plate taught by Brown et al into a controlled-atmosphere chamber since Brown et al teach that the device can be used to analyze live cells, and live cells require the proper temperature and gaseous conditions to remain viable. With regards to claim 60, the MALDI sample plate taught by Brown et al is mobile since it capable of being moved. With regards to claim 61, it would have been obvious to one of ordinary skill in the art to place the cells analyzed using the MALDI plate taught by Brown et al into a culture medium so as to ensure that the cells remain viable by having the required nutrients to survive. With regards to claim 62, it would have been obvious to one of ordinary skill in the art to automate the handling of the device taught by Brown et al so as to provide a faster and more convenient analysis with less operator error.

14 Claims 35-39 and 41-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al (EP 1,284,495, submitted in the IDS filed on January 6, 2006) in view of Thomas et al (US 6,632,656). For a teaching of Brown et al, see previous paragraphs in this Office action. Brown et al fail to teach that the planar surface of the support 1 is covered with a film after a sample containing cells is applied thereto for allowing gases to pass through while preventing evaporation of the aqueous solution in which the cells are located.

Thomas et al teach of a device and method for analyzing live cells in a liquid medium. The apparatus comprises a base support having a plurality of microchannels. The microchannels comprise a cell growth chamber and an assay chamber. Upon application of a sample of cells to the device, the cells flow to the cell growth chamber 2 where the cells are cultured. In the cell growth chamber, a gas permeable plastic film or polymer membrane is placed over the cells so as to allow gases such as oxygen needed for metabolism to reach the cells while preventing

evaporation of the culture medium in which the cells are located. Thomas et al teach that the cells in the device can be subjected to a stimulus such as test substances or molecules (i.e. proteins, antibodies, etc) to evaluate the effect of these molecules on the cells. See Figure 1a, lines 12-32 in column 2, lines 10-17 and 65-67 in column 3, lines 1-24 in column 4 and the claims of Thomas et al.

Based upon the combination of Brown et al and Thomas et al, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to provide the planar surface of the support in the device taught by Brown et al with a film after a sample containing cells is applied thereto for allowing gases to pass through while preventing evaporation of the aqueous solution in which the cells are located since Thomas et al teach that such a film on a support holding an aqueous solution of cells serves to keep live cells on the support viable by allowing gases needed for cell growth to pass into and out of the aqueous solution while preventing the aqueous solution from evaporating, and Brown et al teach that the MALDI sample plate can be used to analyze live cells. With regards to claims 36-37 and 41-42, it would have been obvious to one of ordinary skill in the art to subject the cells taught by Brown et al on the MALDI sample plate to a stimulus such as a reagent molecule since Thomas et al teach that the interaction of cells with different molecules can be advantageously screened using a planar support-type of device, similar to the MALDI plate taught by Brown et al. With regards to claims 52-54, it would have been obvious to one of ordinary skill in the art to place the MALDI sample plate taught by Brown et al into a controlled-atmosphere chamber since Brown et al teach that the device can be used to analyze live cells, and live cells require the proper temperature and gaseous conditions to remain viable. With regards to claim 60, the MALDI sample plate taught

by Brown et al is mobile since it capable of being moved. With regards to claim 61, it would have been obvious to one of ordinary skill in the art to place the cells analyzed using the MALDI plate taught by Brown et al into a culture medium so as to ensure that the cells remain viable by having the required nutrients to survive. With regards to claim 62, it would have been obvious to one of ordinary skill in the art to automate the handling of the device taught by Brown et al so as to provide a faster and more convenient analysis with less operator error.

15. Claim 40 is rejected under 35 U.S.C. 103(a) as being unpatentable over either Brown et al in view of Schaack et al or Brown et al in view of Thomas et al as applied to claims 35-39 and 41-69 above, and further in view of Applicants' admitted prior art in the specification. For a teaching of Brown et al, Schaack et al and Thomas et al, see previous paragraphs in this Office action. Brown et al fail to teach that a piezoelectric system can be used to deposit the solution of cells or other biomolecules onto the planar support of the MADLI plate.

Applicants admit on page 19 of the specification that the use of piezoelectric systems to dispense solutions of cells and reagents onto substrates such as DNA chips are conventional. See the first paragraph on page 19 of the instant specification.

Based upon the combination of either Brown et al, Schaack et al and Applicants' admitted prior art or Brown et al, Thomas et al and Applicants' admitted prior art, it would have been obvious to one of ordinary skill in the art to use a piezoelectric system to deposit the solution of cells and other biomolecules onto the planar support of the MALDI plate taught by Brown et al since Applicants admit that such piezoelectric systems are conventionally known for such a purpose, and therefore, there is nothing inventive in using a piezoelectric system in conjunction with the device taught by Brown et al.

16. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Please make note of: Palander who teach of a method for treating cell samples on a slide using a evaporation inhibitor liquid; Engelking et al who teach of a surface for analyzing biochemical samples using mass spectrometry; Franzen et al, Clark et al, Jarrell et al, Schurenberg et al and Perreault et al who teach of sample supports for MALDI mass spectrometry.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maureen M. Wallenhorst whose telephone number is 571-272-1266. The examiner can normally be reached on Monday-Thursday from 6:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vickie Kim, can be reached on 571-272-0579. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maureen M. Wallenhorst
Primary Examiner
Art Unit 1797

mmw

September 17, 2009

/Maureen M. Wallenhorst/

Primary Examiner, Art Unit 1797